Atty. Dkt. No. ABI1550-1
(071243-1404)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Patrick Soon-Shiong et al.

Title: LONG TERM ADMINISTRATION OF PHARMACOLOGICALLY ACTIVE AGENTS

Appl. No.: 09/937,840

Filing Date: 01/28/2002

Examiner: C. Delacroix-Muirheid

Art Unit: 1614

Conf No. 7072

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I hereby certify that this paper is being facsimile transmitted to the United States Patent and Trademark Office, Washington, D.C. on the date below.

Stephen E. Reiter
(Printed Name)

(Signature)

January 22, 2004
(Date of Deposit)

RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Responsive to the Office Action mailed December 22, 2003, please consider the following amendments and remarks.

Amendments to the Claims are included in the **Listing of Claims** which begins on page 2 of this paper.

Remarks begin on page 6 of this paper.

LISTING OF CLAIMS

Please add claims 18-21 as follows. This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Original) A method for the treatment of a subject having an infirmity, said method comprising administering to said subject a sub-therapeutic dose level of a pharmacologically active agent effective against said infirmity.

2. (Original) A method according to claim 1, wherein said pharmacologically active agent is selected from the group consisting of chemotherapeutic drugs, taxanes, epitholones, agents which modify microtubule activity or assembly, small molecule drugs, biologics, peptides, antibodies, enzymes, antisense therapeutics, polynucleotides, synthetic polynucleotide constructs, antiinfectives, antirejection drugs, analgesics/antipyretics, anesthetics, antiasthmatics, antibiotics, antidepressants, antidiabetics, antifungal agents, antihypertensive agents, anti-inflammatories, antineoplastics, antianxiety agents, immunosuppressive agents, antimigraine agents, sedatives/hypnotics, antianginal agents, antipsychotic agents, antimanic agents, antiarrhythmics, antiarthritic agents, antigout agents, anticoagulants, thrombolytic agents, antifibrinolytic agents, hemorheologic agents, antiplatelet agents, anticonvulsants, antiparkinson agents, antihistamines/antipruritics, agents useful for calcium regulation, antibacterial agents, antiviral agents, antimicrobials, anti-infectives, bronchodialators, hormones, hypoglycemic agents, hypolipidemic agents, proteins, nucleic acids, agents useful for erythropoiesis stimulation, antiulcer/antireflux agents, antinauseants/antiemetics, oil-soluble vitamins, mitotane, visadine, halonitrosoureas, anthrocyclines, and ellipticine.

3. (Original) A method according to claim 1, wherein said pharmacologically active agent is administered by one or more routes of administration selected from the group consisting of topical, oral, intraarticular, intracisternal, intraocular, intraventricular,

intrathecal, intravenous, intramuscular, intraperitoneal, intradermal/transdermal/subcutaneous, intratracheal/inhalational, rectal, vaginal, intracranial, intraurethral, intrahepatic, intraarterial, intratumoral, and mucosal.

4. (Original) A method according to claim 1, wherein said pharmacologically active agent is administered systemically.

5. (Original) A method according to claim 1, wherein said pharmacologically active agent is administered locally.

6. (Original) A method according to claim 1, wherein said sub-therapeutic dose is administered over an administration time in the range from about 2 days to about 1 year.

7. (Original) A method according to claim 1, wherein said sub-therapeutic dose is administered over an administration time in the range from about 7 days to about 9 months.

8. (Original) A method according to claim 1, wherein said sub-therapeutic dose is administered over an administration time in the range from about 2 weeks to about 3 months.

9. (Original) A method according to claim 1 wherein said infirmity is breast cancer, ovarian cancer, lung cancer, hepatic disease, brain disease, bladder cancer or prostate cancer.

10. (Original) A method according to claim 1 wherein said subject is a human.

11. (Original) A method for eliminating cancer cells in a subject having said cancer cells, said method comprising administering to said subject a sub-therapeutic dose level of an antineoplastic agent.

12. (Original) A method according to claim 11 wherein said antineoplastic agent is paclitaxel.

13. (Original) A method for administration of a pharmacologically active agent to a subject in need thereof so as to achieve therapeutic levels thereof for more than 4 days, said method comprising regularly administering said pharmacologically active agent at a sub-therapeutic dose level for greater than 4 days.

14. (Original) A method for administration of a pharmacologically active agent to a subject in need thereof without subjecting said subject to adverse events caused by higher than therapeutic levels of said pharmacologically active agent, said method comprising regularly administering said pharmacologically active agent at a sub-therapeutic dose level for a time sufficient to achieve a therapeutic effect.

15. (Original) A unit dosage form for the treatment of a subject having an infirmity, said unit dosage form comprising a sub-therapeutic dose level of a pharmacologically active agent effective against said infirmity.

16. (Original) A unit dosage form according to claim 15, wherein the pharmacologically active agent in the unit dosage form is selected from the group consisting of chemotherapeutic drugs, taxanes, epitholones, agents which modify microtubule activity or assembly, small molecule drugs, biologics, peptides, antibodies, enzymes, antisense therapeutics, polynucleotides, synthetic polynucleotide constructs, antiinfectives, antirejection drugs, analgesics/antipyretics, anesthetics, antiasthmatics, antibiotics, antidepressants, antidiabetics, antifungal agents, antihypertensive agents, anti-inflammatories, antineoplastics, antianxiety agents, immunosuppressive agents,

antimigraine agents, sedatives/hypnotics, antianginal agents, antipsychotic agents, antimanic agents, antiarrhythmics, antiarthritic agents, antigout agents, anticoagulants, thrombolytic agents, antifibrinolytic agents, hemorheologic agents, antiplatelet agents, anticonvulsants, antiparkinson agents, antihistamines/antipruritics, agents useful for calcium regulation, antibacterial agents, antiviral agents, antimicrobials, anti-infectives, bronchodialators, hormones, hypoglycemic agents, hypolipidemic agents, proteins, nucleic acids, agents useful for erythropoiesis stimulation, antiulcer/antireflux agents, antinauseants/antiemetics, oil-soluble vitamins, mitotane, visadine, halonitrosoureas, anthrocyclines, and ellipticine.

17. (Original) A unit dosage form according to claim 15, wherein the pharmacologically active agent is administered by one or more routes of administration selected from the group consisting of topical, oral, intraarticular, intracisternal, intraocular, intraventricular, intrathecal, intravenous, intramuscular, intraperitoneal, intradermal/transdermal/subcutaneous, intratracheal/inhalational, rectal (i.e., via suppository), vaginal (i.e., via pessary), intracranial, intraurethral, intrahepatic, intraarterial, intratumoral, and mucosal.

18. (New) A method according to claim 1, wherein said pharmacologically active agent is a chemotherapeutic drug.

19. (New) A method according to claim 1, wherein said pharmacologically active agent is administered intravenously.

20. (New) A unit dosage form according to claim 15, wherein the pharmacologically active agent in the unit dosage form is a chemotherapeutic drug.

21. (New) A unit dosage form according to claim 15, wherein the pharmacologically active agent is administered intravenously.

REMARKS

The present invention relates to methods for the treatment of a subject having an infirmity. Invention methods are broadly applicable to the administration of a wide variety of pharmacologically active agents, and can be implemented by a variety of routes of administration. Invention methods comprise administering to a subject a sub-therapeutic dose level of a pharmacologically active agent (such as the anticancer agent paclitaxel) effective against an infirmity over an administration period sufficient to achieve a therapeutic effect.

By the present communication, claims 18-21 have been introduced to define Applicants' invention with greater particularity and not in response to any prior art. This amendment does not introduce new matter as it is fully supported throughout the specification and claims as originally filed. Accordingly, Claims 1-21 are now pending in this application. The present status of all claims in the application is provided in the listing of claims presented herein beginning on page 2.

Elections/Restrictions

The restriction of claims 1-17 under PCT Rule 13.1, is respectfully traversed. It is respectfully submitted that invention methods are broadly applicable to the administration of a wide variety of pharmacologically active agents, and can be implemented by a variety of routes of administration. Given the broad applicability of the invention methods, it is respectfully submitted that Applicants are entitled to claims of broad scope. Accordingly, restriction as asserted by the Examiner is improper. Moreover, to limit the scope of a single application as suggested by the asserted lack of unity would be unduly burdensome to the Applicant.

Furthermore, a thorough search of claims directed to methods for treating a subject having an infirmity by administering a sub-therapeutic dose level of a pharmacologically active agent such as a chemotherapeutic agent, would, of necessity, include a search of

agents such as taxanes, agents which modify microtubule activity or assembly, antineoplastics, and the like. Accordingly, no savings of Patent Office resources will be achieved if the restriction as asserted is maintained.

Similarly, a thorough search of claims directed to methods for treating a subject having an infirmity employing various routes of administration such as intravenous administration, would, of necessity, include a search of several possible alternative modes of administration, e.g., oral, topical, and the like. Accordingly, no savings of Patent Office resources will be achieved if the restriction as asserted is maintained. Therefore, reconsideration and withdrawal of the requirement for restriction are respectfully requested.

Alternatively, consideration is requested for grouping the various pharmacologically active agents and/or the various modes of administration into a limited number of subsets of the broader categories. For example, pharmacologically active agents such as chemotherapeutic agents, taxanes, antineoplastics, and agents which modify microtubule activity or assembly could readily be examined together. Similarly, pharmacologically active agents such as peptides, antibodies and enzymes could readily be examined together.

As another alternative, it is respectfully submitted that upon election of a single species of pharmacologically active agent, any suitable mode of administration for such agent should be examined in the same application. For example, chemotherapeutics are commonly administered by intravenous, intraarterial, intratracheal/inhalational, oral, intraperitoneal, intratumoral, intrahepatic, topical, intrauretheral, or intracranial routes of administration, and therefore could readily be considered in a single group.

In order to be fully responsive, Applicants hereby elect **chemotherapeutic drugs** as the active agent and elect **intravenous** as the route of administration, both with traverse. All of the pending claims read on the elected species.

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In view of the above amendments and remarks, prompt and favorable action on all claims is respectfully requested. In the event any issues remain to be resolved in view of this communication, the Examiner is invited to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: January 22, 2004

By _____

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